Acute lymphoblastic leukemia is the most common childhood cancer resulting from impaired maturation of white blood cells within bone marrow. Different types of genetic defects accumulating over time in lymphocyte precursor cells may contribute to leukemia development. However, malignant transformation of normal cells into cancer cells may also occur as result of one-time catastrophic event called chromothripsis. This phenomenon is associated with shattering of focal chromosomal region with concomitant impaired rejoining of DNA fragments by dysfunctional DNA repair systems. Some DNA fragments are lost to the cells while others are rearranged and may fuse together leading to aberrant gene function. For instance, gene fusion may promote cell division and in this way favor cancer development.

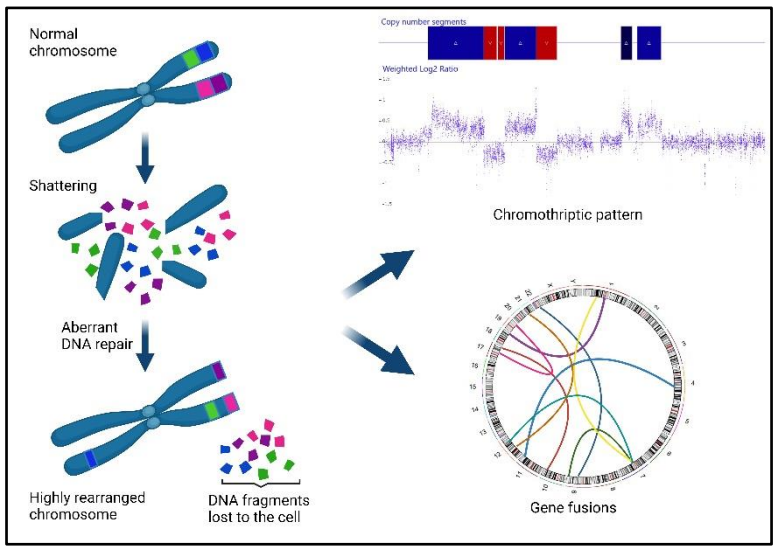

Fig. 1. Schematyczna prezentacja chromotrypsji

Chromothripsis has not been extensively explored in acute lymphoblastic leukemia but some inherited mutations affecting DNA repair genes were indicated as risk factors of its incidence. Chromothripsis has been also described as a poor prognostic marker across different cancer entities related with an increased risk of relapse and a shorter disease-free survival. In this project, we are going to investigate the clinical course of leukemia hallmarked with chromothripsis, molecular background of this phenomenon as well as its biological consequences for cancer cells. To this purpose, we plan to study the presence of genetic abnormalities within the whole genome of leukemic cells and normal cells of the patient who develop this ALL entity. We aim to identify molecular defects which favour the recurrence of leukemia and could become targets for effective treatment of this malignancy.